

of which were previously submitted on December 22, 2000 and received by the US PTO on December 28, 2000. Please enter this sequence listing into the specification of the above-captioned application by amendment as indicated above. The content of the paper and computer readable copies of the Sequence Listing submitted in accordance with 37 C.F.R. §§ 1.821(c) and (e), respectively, are the same and contain new matter.

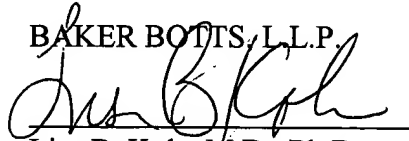
The specification is amended to include sequence identifiers in order to comply with the rules. The specification is also amended to correct obvious and inadvertent errors, to provide updated information regarding the attorney docket number and the software with which it was created, and to eliminate SEQ ID NOS:5 and 6, which were duplicative of SEQ ID NOS:1 and 2. Specifically, line 130 has been amended from "0575/62943" to "34586 (070050.1668)," line 170 has been amended from "PatentIn version 3.0" to "FastSEQ for Windows Version 4.0, rd, line 213 of SEQ ID NOS:1 and 2 have been amended from "RAT" to "Rattus norvegicus," line 213 of SEQ ID NOS:3 and 4 have been amended from "HUMAN" to "homo sapiens," and line 213 of SEQ ID NOS:5 and 6 (formerly SEQ ID NOS:7 and 8) have been amended from "RAT" to "Artificial Sequence." Line 223, indicating that the Artificial Sequence is a synthetic oligonucleotide, has been added to SEQ ID NOS:5 and 6 (formerly SEQ ID NOS:7 and 8).

Further, in reviewing the file of this application, it was noted that, according to a receipt from the American Type Culture Collection ("ATCC"), the plasmids said to be deposited in the specification were not received by the ATCC until August 28, 2000, after the above-identified application was filed, although they were mailed to the ATCC on August 23, 2000 by Federal Express. Accordingly, references to these plasmids have been deleted.

None of these amendments constitutes new matter. Replacement paragraphs marked
to show revisions are attached hereto pursuant to 37 C.F.R. §1.121.

Respectfully submitted,

BAKER BOTTS, L.L.P.



Lisa B. Kole, M.D., Ph.D.

Patent Office Reg. No. 35,225
(212) 408-2628

Anthony Giaccio
Patent Office Registration No. 39,684

Attorneys for Applicants

RECEIVED

JUL 0 8 2002

OFFICE OF PETITIONS



MARKED UP VERSION SHOWING AMENDMENTS

IN THE SPECIFICATION:

Please amend the first paragraph on page 3 lines 3-9 as follows:

Figure 1. Nucleotide (SEQ ID NO:1) and predicted amino acid (SEQ ID NO:2) sequence of the rat PSGen 13 gene (designated PSGen 13). The [S]starting ATG of the open reading frame and the stop codon are bold faced and the poly(A) signal is underlined. [(SEQ ID NOS: ____ and ____) ATCC designation No. _____, which was deposited on August 24, 2000 under the provisions of the Budapest Treaty with the American Type Culture Collection (see details hereinbelow).]

Please amend paragraph 2 on page 3 at lines 11-17 as follows:

Figure 2. Nucleotide (SEQ ID NO:3) and predicted amino acid (SEQ ID NO:4) sequence of the human PSGen 13 gene (designated HuPSGen 13). The [S]starting ATG of the open reading frame and the stop codon are bold faced and the poly(A) signal is underlined. [(SEQ ID NOS: ____ and ____) ATCC designation No. _____, which was deposited on August 24, 2000 under the provisions of the Budapest Treaty with the American Type Culture Collection (see details hereinbelow).]

Please amend paragraph 3 on page 3 at lines 19-22 as follows:

Figure 3. Nucleotide sequence comparison between the rat PSGen 13 (SEQ ID NO:5) and HuPSGen 13 (SEQ ID NO:6) cDNAs. The start and stop codons of the rat PSGen 13 and HuPSGen 13 genes are underlined. [(SEQ ID NOS: ____ and ____).]

Please amend paragraph 4 on page 3 at lines 24-27 as follows:

Figure 4. Amino acid sequence comparison between the rat PSGen 13 (SEQ ID NO:2) and HuPSGen 13 (SEQ ID NO:4) encoded proteins. Conserved substitutions in the rat PSGen 13 and HuPSGen 13 proteins are underlined. [(SEQ ID NOS: _____ and _____).]

Please amend paragraph 5 on page 3 line 29 through page 4 line 9 as follows:

Figure 5. Differential expression of PSGen[-]_13 identified by RSDD and reverse Northern blotting in a large panel of rodent cells displaying differences in transformation progression. A Northern blot of cells displaying various stages of transformation progression was probed with a radiolabeled [³²P] rat PSGen 13 cDNA initially identified by RSDD and reverse Northern blotting (6). The cell types used include unprogressed E11 (-), CREF X E11-NMT F1 (-) and CREF X E11-NMT F2 (-) somatic cell hybrids, E11 X E11-NMT A6 (-) somatic cell hybrid, E11 X E11-NMT 3b (-) somatic cell hybrid, and E11-NMT AZA B1 (-) and E11-NMT AZA C1 (-) 5-azacytidine-treated E11-NMT clones; and progressed E11-NMT (+), CREF X E11-NMT R1 (+) and CREF X E11-NMT R2 (+) somatic cell hybrids, E11 X E11-NMT A6TD (+) nude mouse tumor derived somatic cell hybrid, E11 X E11-NMT IIa (+), E11-Ras R12 (+) and E11-HPV E6/E7 (+) and an E11 clone transformed by the E6 and E7 region of HPV-18. Equal loading of RNAs is demonstrated by ethidium bromide (EtBr) staining. Data from ref. 6.

Please amend the second full paragraph on page 6 at lines 12-28 as follows:

The invention provides for an isolated nucleic acid encoding a Progression Suppressed Gene 13 (PSGen 13) protein. In one embodiment of the invention, the [Progression Suppressed
NY02:381108.2

Gene 13 ([PSGen 13]) protein is a human protein, a rat protein, a primate protein, a mouse protein, or a bovine protein. In another embodiment of the invention, the nucleic acid comprises the polynucleotide sequence shown in SEQ ID NO:1. In another embodiment of the invention, the nucleic acid comprises the polynucleotide sequence in SEQ ID NO:[2]3. In another embodiment of the invention, the nucleic acid consists essentially of the polynucleotide sequence shown in SEQ ID NO:1. In another embodiment of the invention, the nucleic acid consists essentially of the polynucleotide sequence shown in SEQ ID NO:[2]3. In another embodiment of the invention, the nucleic acid consists of the polynucleotide sequence shown in SEQ ID NO:1. In another embodiment of the invention, the nucleic acid consists of the polynucleotide sequence shown in SEQ ID NO:[2]3.

Please amend the second full paragraph on page 8 at lines 8-16 as follows:

The invention provides for an isolated nucleic acid encoding a Progression Suppressed Gene 13 (PSGen 13) protein. In one embodiment of the invention, the protein is a human protein, a rat protein, a primate protein, a mouse protein, or a bovine protein. In another embodiment of the invention, the protein has a polypeptide sequence which is encoded by the polynucleotide sequence shown in SEQ ID NO:1. In another embodiment of the invention, the protein has a polypeptide sequence which is encoded by the polynucleotide sequence shown in SEQ ID NO:[2]3.

Please delete the first and second full paragraphs, lines 8-22 and 24-35, respectively, from page 10.

[Biological Deposit

NY02:381108.2

The invention provides for a nucleic acid encoding PSGen 13 (rat) protein, which nucleic acid, designated PSGen 13, ATCC Designation No. _____, deposited August 24, 2000 with the American Type Culture Collection (ATCC), 10801 University Blvd, Manassas, Virginia, 20110-2209 under the provision of the Budapest Treaty for the International Recognition of the Deposit of Microorganism for the Purpose of Patent Procedure. This deposit is an insert within a plasmid vector, pcDNA3.1(+). It is within the EcoRI-Xho I cloning site. The insert is about 0.8 kb in length. The sense strand promoter of the plasmid is T7. The plasmid carries resistance genes to ampicillin and neomycin. The insert origin is EST clone #2005777. The rat tissue used to isolate the DNA was the adrenal gland tissue.

The invention provides for a nucleic acid encoding HuPSGen 13 (human) protein, which nucleic acid, designated PSGen 13, ATCC Designation No. _____, deposited August 24, 2000 with the American Type Culture Collection (ATCC), 10801 University Blvd, Manassas, Virginia, 20110-2209 under the provision of the Budapest Treaty for the International Recognition of the Deposit of Microorganism for the Purpose of Patent Procedure. This deposit is an insert within a plasmid vector, pT7T-Pac. It is within the EcoRI-Not I cloning site. The insert is about 0.83 kb in length. The plasmid carries a resistance gene to ampicillin. The insert origin is EST clone #2525262. The human tissue used to isolate the DNA was human kidney tissue.]

Please amend the first full paragraph on page 33, line 30 bridging to page 34, line

10, as follows:

NY02:381108.2

Construction of PSGen 13-expressing E11-NMT clones. E11-NMT and DU-145 cells were transfected with a pcDNA3.1[](+) expression vector (containing a neomycin resistance gene) lacking or having the complete PSGen 13 gene as previously described (11). Briefly, 1[]x[]10⁵ cells were seeded in 10-cm tissue culture plates[.]. [6]Six hr later, 10 []μg of purified pcDNA3.1[](+) vector or a rat PSGen 13/pcDNA3.1[](+) construct was incubated with 30 μl of Lipofectamine (Gibco BRL) and this mixture was added to the cells for 8 hr. The next day the media was changed, with the addition of 500 μg/ml of G418. [and]Thereafter, the media was changed 2X per week for three weeks. G418-resistant colonies were isolated using cloning cylinders and maintained as independent cell lines, referred to as NMT-PSG13 clones (cl 3, 5, 6, 7, 8, 9, 10, 11 and 12) and DU-PSG13 clones (cl 11, 12, 13, 14, 15 and 17), in complete media containing 100 μg/ml of G418. Additionally, NMT-vector and DU-145-Vec clones were isolated and maintained as independent cell lines in complete media containing 100 μg/ml of G418.

Please amend the first full paragraph on page 35 at lines 10-24 as follows:

Cloning a full length rat PSGen 13 and HuPSGen 13 cDNA. An original rat PSGen 13 EST was identified using RSDD and reverse Northern hybridization as a gene displaying elevated expression in E11 versus E11-NMT cells (6). A full length open reading frame (ORF) of rat PSGen 13 was cloned using the complete open reading frame (C-ORF) approach with specific gene primers (20) and electronic data mining based on the EST sequence. Primers used for C-ORF were PSGen13-R2 (5'-TCG CTT CTC ACT TTG ACG GAG TGT CAA G-3') (SEQ ID NO:7) and PSGen13-R2 Nested (5'-TGT CAA GTG TGG CAG AGA CTA AGA ATG G-3') (SEQ ID NO:8). In addition, full length rat PSGen 13 and NY02:381108.2

HuPSGen 13 cDNA clones were identified by sequence comparison of the rat PSGen 13 EST with GenBank by BLAST. Selected clones (ATCC #200577 from rat PSGen 13 and ATCC #2525262 for HuPSGen_13) were procured (Research Genetics) and sequenced.

Please amend the paragraph bridging pages 35 and 36 at page 35 line 28 through page 36 line 7 as follows:

Sequence Informatics of PSGen 13. The cloned full length rat PSGen 13 cDNA consists of 780 bp excluding the poly(A) tail. A poly(A) signal (AATAAA) is located at position 763 (Fig. 1) (SEQ ID NO:1). The ORF starts at the first ATG at 170 bp, which is preceded [followed]by an in-frame stop codon at 86 bp, and spans to 415 bp. Rat PSGen 13 encodes a protein with predicted 81 amino acids of calculated molecular weight of 9 kDa with a pI of 5.52 (Fig. 1). Protein sequence analysis did not indicate hydrophobic patches for membrane spanning regions of signal peptide sequences characteristic of secretory proteins. Motif and pattern analysis also failed to identify sequence homologies with previously reported genes, information that is useful in providing potential insights into the biological function and or mode of action of rat PSGen13. Based on this observation, rat PSGen13 appears to encode a novel class of proteins.

Please amend the first full paragraph on page 36 at lines 9-31 as follows:

A human homologue of Rat PSGen 13 (HuPSGen 13) was electronically cloned by analyzing sequences reported in the GenBank data base (Fig. 2) (SEQ ID NO:3). HuPSGen 13 is 75% identical to rat PSGen 13 at the nucleotide level, but 94% identical to Rat PSGen 13 on a protein level (7[9]6/81). (Figs. 3 and 4). Of the 5 residues that are distinct in HuPSGen 13, NY02:381108.2

three of them (D at 4, K at 38 and I at 77) are conserved substitutions of rat PSGen 13 (E at 4, R at 38 and V at 77, respectively), which suggests strong conservation in functionality. Furthermore, sequence identity of HuPSGen 13 with rat PSGen 13 protein is 87% at the nucleotide level. Both 5' and 3' untranslated regions display 68.7% and 68.3% identity, respectively, and are more diverse between rat PSGen 13 and HuPSGen 13 than the ORF, which is not uncommon between interspecies homologues. Considering the degree of conservation in the ORF and resulting protein sequence, HuPSGen 13 is an orthologue of rat PSGen 13. The cloned HuPSGen 13 cDNA consists of 835 bp excluding the poly(A) tail and the canonical poly(A) signal was observed at 814 bp. Although an in-frame stop codon was not present, the ORF of HuPSGen 13 starts at the first ATG (197 bp) and runs through 442 bp. HuPSGen 13 encodes 81 amino acids of calculated Mol. Wt. of 9 kDa with a pI of 5.86. As in rat PSGen 13, computational protein analysis did not yield any known functional motifs.

IN THE CLAIMS:

Please amend Claims 4, 6, 8 and 25 to read as follows:

4. (Amended) The isolated nucleic acid of claim 1, wherein the nucleic acid comprises the polynucleotide sequence shown in SEQ ID NO:[2]3.
6. (Amended) The isolated nucleic acid of claim 1, wherein the nucleic acid consists essentially of the polynucleotide sequence shown in SEQ ID NO:[2]3.
8. (Amended) The isolated nucleic acid of claim 1, wherein the nucleic acid consists of the polynucleotide sequence shown in SEQ ID NO:[2]3.
25. (Amended) The protein of claim 22, wherein the protein has a polypeptide
NY02:381108.2

sequence which is encoded by the polynucleotide sequence of SEQ ID NO:[2]3.